

Notice of Allowability	Application No.	Applicant(s)	
	09/997,585	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4/17/06.
2. ☒ The allowed claim(s) is/are 119-123 (renumbered as 1-5, respectively).
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|--|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ | 7. <input type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

EXAMINER'S COMMENT

Reasons for Allowance:

The claims of the instant invention are directed to an isolated antibody that specifically binds to the polypeptide of SEQ ID NO:399. The specification provides several asserted utilities at pages 258-260 and pages 539-557, including that the PRO polypeptides of the present invention may be differentially expressed in a diseased tissue as compared to a normal tissue of the same tissue type.

Applicant states at pages 3-4 of their response (17 April 2006) that Example 170, in the specification sets forth a gene amplification assay, which shows that the PRO1187 gene is amplified in the genome of certain human lung cancers. Applicant states that the gene encoding PRO1187 showed significant amplification, ranging from 2.25-fold to 2.928-fold in different squamous lung tumors. At pages 9-10 of the response, Applicant states that patentable utility for the PRO1187 polypeptides is based upon the gene amplification data for the gene encoding the PRO1187 polypeptide. Example 170 describes the results obtained using a very well-known and routinely employed polymerase chain reaction (PCR)-based assay, the TaqMan PCR assay, also referred to herein as the gene amplification assay. Applicant states that this assay allows one to quantitatively measure the level of gene amplification in a given sample, such as a tumor extract or cell line. Applicant states that genomic DNA was isolated from a variety of primary cancers and cancer cell lines. Applicant argues that tumor samples were tested in triplicates with Taqman primers with internal controls, beta-actin

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and GADPH in order to quantitatively compare DNA levels between samples. As a negative control, DNA was isolated from the cells of normal healthy individuals. Example 170 demonstrates that DNA62876-1517 (PRO1187) was shown to be more highly expressed in primary tumor (human lung tumor; LT12, LT15 and LT16; 2.25 fold to 2.928-fold; page 554) as compared to normal tissue in this Example. Applicant relies on Orntoft *et al.*, Hyman *et al.* and Pollack *et al.* (references of record) to demonstrate that expression levels of mRNA, measured by quantitative PCR, were found to have a good correlation to the expressed protein levels.

It had been argued in the previous Office actions that mRNA levels were not predictive of protein levels, citing references by Hu *et al.* and Haynes *et al.* However, these references were measuring and analyzing mRNA levels using microarrays, not using quantitative PCR analysis and the art recognizes that the results obtained by microarray are not always the same as the results obtained using quantitative PCR (for example, see Oda *et al.*, Virchows Arch. 430:99-105, 1997, specifically page 104, column 1, paragraph 2). While the PTO found several references in which the protein expression levels did not correlate with mRNA levels measured by quantitative PCR (see Sugg *et al.*, Clinical Endocrinology 49:629-637, 1998; Toler *et al.*, Am. J. Obstet. Gynecol. 194:e27-e31, 2006; Berner *et al.* Histopathol. 42:546-554, 2003 ; Brooks *et al.* Am. J. Physiol. Renal Physiol. 284:F218-F228, 2003), the majority of the references which were found, including those cited by Applicant, demonstrated a correlation between mRNA levels measured by quantitative PCR and protein expression levels.


The prior art of record argued by the Examiner is not specifically directed to message levels measured by rtPCR. Based on the totality of evidence of record, one of skill in the art would find it more likely than not that an increase in message as measured by rtPCR would be predictive of an increase in protein expression levels, absent evidence to the contrary. Therefore, the data presented in Example 170, which demonstrates differential expression of nucleic acids encoding PRO1187, also supports a conclusion of differential expression of the PRO1187 polypeptide. Therefore, one of ordinary skill in the art would be able to use an antibody directed to PRO1187 polypeptide diagnostically for distinguishing lung tumor from normal tissue, as asserted by Applicant.

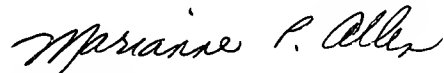
Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


RMD
8/1/06


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